

101 243

## ONLINE SEARCH REQUEST FORM

\*\*\*\*\*

USER Irene M. A.SERIAL NUMBER 09/980453ART UNIT 1651

PHONE \_\_\_\_\_

DATE 8/13/03

Please give a detailed statement of requirements. Describe as specifically as possible the subject matter to be searched. Define any terms that may have special meaning. Give examples or relevant citations, authors, or keywords, if known.

You may include a copy of the broadest and or relevant claim(s).

Please search inventors  
Microbial production of L-epi-2-inosare  
from myo-inositol  
Microbial production of epi-inositol  
from L-epi-2-inosare  
with bacteria of Cl. 12  
" " " 13

BEST AVAILABLE COPY

## STAFF USE ONLY

COMPLETED 8/18/03  
SEARCHER H. M. A.  
ONLINE TIME 1.1 TOTAL TIME 1.1  
(in minutes)  
NO. OF DATABASES \_\_\_\_\_

SYSTEMS  
5475 CAS ONLINE  
\_\_\_\_ DARC/QUESTEL  
\_\_\_\_ DIALOG  
\_\_\_\_ SDC  
\_\_\_\_ OTHER

=&gt; file caplus

FILE 'CAPLUS' ENTERED AT 15:29:05 ON 18 AUG 2003

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FILE COVERS 1907 - 18 Aug 2003 VOL 139 ISS 8

FILE LAST UPDATED: 17 Aug 2003 (20030817/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=&gt; d que 117

L13 1 SEA FILE=REGISTRY ABB=ON PLU=ON EPI-2-INOSOSE/CN

L16 24 SEA FILE=CAPLUS ABB=ON PLU=ON L13

L17 1 SEA FILE=CAPLUS ABB=ON PLU=ON L16(L)(BPN OR BMF)/RL ← any preparation of epi-2-inosose by biological means (micro organism)

=&gt; d que 126

L13 1 SEA FILE=REGISTRY ABB=ON PLU=ON EPI-2-INOSOSE/CN

L15 1 SEA FILE=REGISTRY ABB=ON PLU=ON EPI-INOSITOL/CN

L16 24 SEA FILE=CAPLUS ABB=ON PLU=ON L13

L23 102 SEA FILE=CAPLUS ABB=ON PLU=ON L15

L24 10 SEA FILE=CAPLUS ABB=ON PLU=ON L23(L)PREP/RL ← prep (any means) of epi-inositol

L25 7 SEA FILE=CAPLUS ABB=ON PLU=ON L16(L)(RCT OR RACT)/RL ← epi-2-inosose as a react-

L26 1 SEA FILE=CAPLUS ABB=ON PLU=ON L24 AND L25 1 cite ant

=&gt; s 117 or 126

L81 1 L17 OR L26 1 cite (applicant)

=&gt; file casreact

FILE 'CASREACT' ENTERED AT 15:29:08 ON 18 AUG 2003

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FILE CONTENT:1907 - 17 Aug 2003 VOL 139 ISS 7

Some records from 1974 to 1991 are derived from the ZIC/VINITI data file and provided by InfoChem and some records are produced using some INPI data from the period prior to 1986.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Crossover limits have been increased. See HELP RNCROSSOVER for details.

Structure search limits have been raised. See HELP SLIMIT for the new, higher limits.

=> d que 136

L34	1 SEA FILE=CASREACT ABB=ON	PLU=ON	6623-68-3/PRO	<i>← prep of epi-2-inosose          ← prep of epi-inositol          2 cites</i>	<i>} any means</i>
L35	2 SEA FILE=CASREACT ABB=ON	PLU=ON	488-58-4/PRO		
L36	2 SEA FILE=CASREACT ABB=ON	PLU=ON	(L34 OR L35)		

=> file uspatful

FILE 'USPATFULL' ENTERED AT 15:29:09 ON 18 AUG 2003  
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 14 Aug 2003 (20030814/PD)  
FILE LAST UPDATED: 14 Aug 2003 (20030814/ED)  
HIGHEST GRANTED PATENT NUMBER: US6606748  
HIGHEST APPLICATION PUBLICATION NUMBER: US2003154532  
CA INDEXING IS CURRENT THROUGH 14 Aug 2003 (20030814/UPCA)  
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 14 Aug 2003 (20030814/PD)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2003  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2003

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que 170

L14	1 SEA FILE=REGISTRY ABB=ON	PLU=ON	MYO-INOSITOL/CN
L58	31 SEA FILE=USPATFULL ABB=ON	PLU=ON	?INOSOSE
L59	1910 SEA FILE=USPATFULL ABB=ON	PLU=ON	MYO-INOSITOL OR L14
L65	7 SEA FILE=USPATFULL ABB=ON	PLU=ON	L58(P)L59
L66	1 SEA FILE=USPATFULL ABB=ON	PLU=ON	L65(P)(MICROB? OR MICROORG?)
L67	4 SEA FILE=USPATFULL ABB=ON	PLU=ON	L65(P)(OXIDI? OR OXIDA?)
L68	3 SEA FILE=USPATFULL ABB=ON	PLU=ON	L65 AND (PSEUDOMONAS OR XANTHOMONAS OR ACETOBACTER OR GLUCONOBACTER OR AGROBACTER? OR ERWINIA OR ENTEROBACTER OR SERRATIA OR YERSINIA OR PASTEURELLA OR HAEMOPHIL?)
L69	0 SEA FILE=USPATFULL ABB=ON	PLU=ON	L65 AND FERM(W)BP(W)(7168 OR 7170 OR 7169 OR 10135 OR 10215 OR 10119)
L70	5 SEA FILE=USPATFULL ABB=ON	PLU=ON	(L66 OR L67 OR L68 OR L69) <i>5 cites</i>

=> d que 177

L15	1 SEA FILE=REGISTRY ABB=ON	PLU=ON	EPI-INOSITOL/CN
L58	31 SEA FILE=USPATFULL ABB=ON	PLU=ON	?INOSOSE
L60	49 SEA FILE=USPATFULL ABB=ON	PLU=ON	EPI-INOSITOL OR L15
L76	3 SEA FILE=USPATFULL ABB=ON	PLU=ON	(REDUC? OR BOROHYDRID?) AND L58 AND L60
L77	2 SEA FILE=USPATFULL ABB=ON	PLU=ON	L76 NOT VANADIUM/TI <i>2 cites</i>

=> s 170 or 177

L82 6 L70 OR L77 *6 patents*

=> file scisearch

FILE 'SCISEARCH' ENTERED AT 15:29:12 ON 18 AUG 2003  
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FILE COVERS 1974 TO 15 Aug 2003 (20030815/ED)

=&gt; d que 156

L49 30 SEA FILE=SCISEARCH ABB=ON PLU=ON EPI-INOSITOL  
 L55 59 SEA FILE=SCISEARCH ABB=ON PLU=ON ?INOSOSE  
 L56 2 SEA FILE=SCISEARCH ABB=ON PLU=ON L55 AND L49 *2 cites Sci Search*

=&gt; file wpix

FILE 'WPIX' ENTERED AT 15:29:13 ON 18 AUG 2003  
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FILE LAST UPDATED: 13 AUG 2003 <20030813/UP>  
 MOST RECENT DERWENT UPDATE: 200352 <200352/DW>  
 DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

&gt;&gt;&gt; NEW WEEKLY SDI FREQUENCY AVAILABLE --&gt; see NEWS &lt;&lt;&lt;

>>> SLART (Simultaneous Left and Right Truncation) is now  
 available in the /ABEX field. An additional search field  
 /BIX is also provided which comprises both /BI and /ABEX <<<

&gt;&gt;&gt; PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY &lt;&lt;&lt;

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 SEE <http://www.derwent.com/dwpi/updates/dwpcov/index.html> <<<

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[http://www.derwent.com/userguides/dwpi\\_guide.html](http://www.derwent.com/userguides/dwpi_guide.html) <<<

=&gt; d que 139

L37 245 SEA FILE=WPIX ABB=ON PLU=ON MYO-INOSITOL  
 L38 2 SEA FILE=WPIX ABB=ON PLU=ON EPI-2-INOSOSE  
 L39 1 SEA FILE=WPIX ABB=ON PLU=ON L37 AND L38

=&gt; d que 141

L38 2 SEA FILE=WPIX ABB=ON PLU=ON EPI-2-INOSOSE  
 L40 10 SEA FILE=WPIX ABB=ON PLU=ON EPI-INOSITOL  
 L41 2 SEA FILE=WPIX ABB=ON PLU=ON L40 AND L38

=&gt; d que 142

L38 2 SEA FILE=WPIX ABB=ON PLU=ON EPI-2-INOSOSE  
 L40 10 SEA FILE=WPIX ABB=ON PLU=ON EPI-INOSITOL  
 L41 2 SEA FILE=WPIX ABB=ON PLU=ON L40 AND L38  
 L42 1 SEA FILE=WPIX ABB=ON PLU=ON L41 AND BOROHYDRIDE

=&gt; s 139 or 141-42

L83 2 L39 OR (L41 OR L42) *2 cites WPIX*

=> dup rem 181 136 182 156 183 *removing duplicates*  
 FILE 'CAPLUS' ENTERED AT 15:30:17 ON 18 AUG 2003  
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FILE 'CASREACT' ENTERED AT 15:30:17 ON 18 AUG 2003  
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FILE 'USPATFULL' ENTERED AT 15:30:17 ON 18 AUG 2003  
 CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'SCISEARCH' ENTERED AT 15:30:17 ON 18 AUG 2003  
 COPYRIGHT 2003 THOMSON ISI

FILE 'WPIX' ENTERED AT 15:30:17 ON 18 AUG 2003  
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PROCESSING COMPLETED FOR L81  
 PROCESSING COMPLETED FOR L36  
 PROCESSING COMPLETED FOR L82  
 PROCESSING COMPLETED FOR L56  
 PROCESSING COMPLETED FOR L83

L84 10 DUP REM L81 L36 L82 L56 L83 (3 DUPLICATES REMOVED) *10 cites total*  
 ANSWER '1' FROM FILE CAPLUS  
 ANSWER '2' FROM FILE CASREACT  
 ANSWERS '3-8' FROM FILE USPATFULL  
 ANSWER '9' FROM FILE SCISEARCH  
 ANSWER '10' FROM FILE WPIX

=> d ibib abs hitstr 1

L84 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2000:881342 CAPLUS

DOCUMENT NUMBER: 134:42384

TITLE: Novel process for producing L-epi-2-inosose by  
 microbial oxidation of myo-inositol and novel process  
 for producing epi-inositol

INVENTOR(S): Takahashi, Atsushi; Kanbe, Kenji; Mori, Tetsuya; Kita,  
 Yuichi; Tamamura, Tsuyoshi; Takeuchi, Tomio

PATENT ASSIGNEE(S): Hokko Chemical Industry Co., Ltd., Japan; Zaidan Hojin  
 Biseibutsu Kagaku Kenkyu Kai

SOURCE: PCT Int. Appl., 65 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

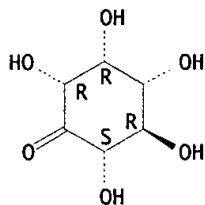
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075355	A1	20001214	WO 2000-JP3687	20000607
W: CA, CN, IL, IN, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1197562	A1	20020417	EP 2000-937174	20000607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:		JP 1999-159861	A	19990607
		JP 1999-340523	A	19991130
		JP 2000-151709	A	20000523
		WO 2000-JP3687	W	20000607

OTHER SOURCE(S): CASREACT 134:42384

AB L-Epi-2-inosose and epi-inositol, which are useful as various drugs or synthesis intermediates; can be efficiently produced from less expensive myo-inositol. Myo-inositol is treated with a gram-neg. bacterium. e.g. Xanthomonas sp., capable of converting myo-inositol into L-epi-2-inosose to thereby convert the myo-inositol into L-epi-2-inosose. The L-epi-2-inosose thus obtained is further reacted in an aq. reaction medium with a reducing agent comprising an alkali metal boron hydride or another alkali metal hydride to form epi-inositol and myo-inositol. Next, the epi-inositol is sepd. and isolated from the redn. reaction mixt.

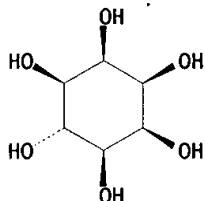
comprising epi-inositol and myo-inositol to give epi-inositol.  
 IT 6623-68-3P, epi-2-Inosose  
 RL: BPN (Biosynthetic preparation); RCT (Reactant);  
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (novel process for producing L-epiinosose by microbial oxidn. of myo-inositol and boron hydride-redn. to epi-inositol)  
 RN 6623-68-3 CAPLUS  
 CN epi-2-Inosose (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 488-58-4P, epi-Inositol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (novel process for producing L-epiinosose by microbial oxidn. of myo-inositol and boron hydride-redn. to epi-inositol)  
 RN 488-58-4 CAPLUS  
 CN epi-Inositol (9CI) (CA INDEX NAME)

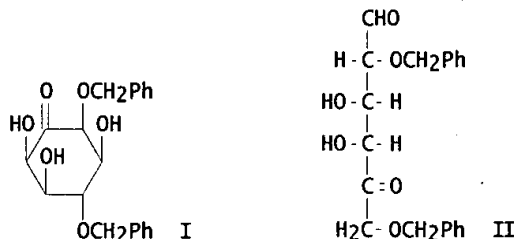
Relative stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

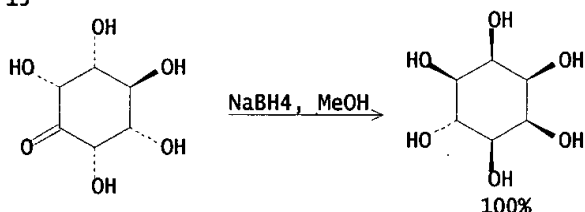
=> d ibib abs fcdref 2

L84 ANSWER 2 OF 10 CASREACT COPYRIGHT 2003 ACS on STN DUPLICATE 2  
 ACCESSION NUMBER: 133:105232 CASREACT  
 TITLE: Rare and complex saccharides from D-galactose and other milk-derived carbohydrates. Part 12. A new highly diastereoselective synthesis of epi-inositol from D-galactose  
 AUTHOR(S): Pistara, Venerando; Barili, Pier Luigi; Catelani, Giorgio; Corsaro, Antonino; D'Andrea, Felicia; Fisichella, Salvatore  
 CORPORATE SOURCE: Dipartimento di Scienze Chimiche, Universita degli Studi di Catania, Catania, I-95125, Italy  
 SOURCE: Tetrahedron Letters (2000), 41(17), 3253-3256  
 CODEN: TELEAY; ISSN: 0040-4039  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB The inosose deriv. I (Bn = PhCH<sub>2</sub>) was obtained with high stereoselectivity by intramol. aldol condensation of the aldohexos-5-ulose II, and it was selectively reduced and debenzylated to give epi-inositol in high yield. The stereochem. and the preferred conformations of the compds. were detd. through 1D- and 2D-NMR expts.

RX(5) OF 13



REF: Tetrahedron Letters, 41(17), 3253-3256; 2000  
NOTE: stereoselective

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitrn kwic 3-8

L84 ANSWER 3 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2002:88660 USPATFULL  
TITLE: Labelled phosphoinositides and analogues  
INVENTOR(S): Aneja, Rajindra, Ithaca, NY, United States  
PATENT ASSIGNEE(S): Nutrimed Biotech, Ithaca, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6376697	B1	20020423
APPLICATION INFO.:	US 1999-292242		19990415 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-81847P	19980415 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Ambrose, Michael G.	
LEGAL REPRESENTATIVE:	Williams, Morgan and Amerson	
NUMBER OF CLAIMS:	29	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	1102	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides novel compounds comprising cellular phosphoinositides and analogues tagged with stable or radioactive isotopes. The present invention also provides novel methods for the

preparation of the said phosphoinositides by syntheses, and novel key intermediates of synthesis; the novel methods of synthesis are applied also for the preparation of the phosphoinositides in non-labelled form. In addition, the present invention discloses a class of novel compounds as isotope labelled key precursors of labelled phosphoinositides. These precursors are derivatives of the target phosphoinositides, labelled with stable or radioactive isotopes, wherein OH and phosphate groups are blocked with temporary protecting groups.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD In the second approach, outlined in Scheme 2, a selectively protected myo-inositol, e.g., 1D-2,6-di-O-benzyl-myo-inositol-3,4,5-tris(dibenzylphosphate) 10, wherein only the equatorial 1-OH is unprotected, and all other OH groups are blocked with temporary protecting groups is a suitable starting material.

Oxidation of 10 (Step a) to the corresponding inosose 11 is carried out using the reagent mixture comprising dimethylsulfoxide and acetic anhydride (DMSO-Ac.sub.2O). A hydrogen, deuterium or tritium atom is introduced (Step b) by reduction of inosose 11, using NaBH.sub.4, NaB.sup.2H.sub.4 or NaB.sup.3H.sub.4, to the corresponding secondary alcohol 12 carrying H--C--OH, .sup.2H--C--OH or .sup.3H--C--OH labels. The product . . . pyridine. The purified product 13 is the labelled precursor analogous with 3, and is deprotected by H.sub.2-Pd/C to labelled 1D-1-(1',2'-O-dipalmitoyl-sn-glycero-3'-phospho)-myo-inositol-3,4,5-trisphosphate (DPPTdIns-3,4,5-P.sub.3) 14. ##STR5##

DETD The phosphatidyl-inosose (7) and inosose (11) employed in Scheme 1 and 2 respectively are important novel intermediates. Equally useful are the 2-phosphatidyl-1-keto and 1-phosphatidyl-6-keto structural isomers of 7 and the 2-keto and 6-keto isomers of 11 prepared by oxidation of the corresponding 1-phosphatidyl-1-OH and 1-phosphatidyl-6-OH compounds. Both phosphatidyl-inosose and inosose types may have temporary protecting groups other than benzyls so as to avoid metal catalyzed hydrogenolysis for deprotection and concomitant reduction of C--C unsaturation in the fattyacyl chains. The present invention discloses novel selectively protected chiral myo-inositol synthons that incorporate temporary protecting groups which are removed without metal catalyzed hydrogenation. In addition, the groups are compatible with the reagents and conditions validated in Schemes 1 and 2 for the oxidation and reduction steps.

DETD Similarly, the 2-phosphatidyl isomer 1D-2-(1',2'-O-dipalmitoyl-sn-glycero-3'-phospho)-3,6-di-O-benzyl-myo-inositol-4,5-bis(dibenzylphosphate) 51 was esterified to 52. Both 49 and 52 formed on oxidation the corresponding inosose derivative, 50 and 53 respectively. These phosphatidyl-inosose esters represent another group of key intermediates for labeling with hydrogen isotopes.

DETD Oxidation of 1D-1-(1',2'-O-dipalmitoyl-sn-glycero-3'-phospho)-3,6-di-O-benzyl-myo-inositol-4,5-bis(dibenzylphosphate) 6 by CrO.sub.3.Py.sub.2 (Procedure A) at r.t. for 5 min was quenched by ice cold aqueous SO.sub.2. The product recovered by evaporation of the organic layer. Purification by chromatography on flash silica using a gradient of CHCl.sub.3--MeOH--NH.sub.4OH gave 1D-1-(1',2'-O-dipalmitoyl-sn-glycero-3'-phospho)-3,6-di-O-benzyl-2-myo-inosose-4,5-bis(dibenzylphosphate) 7 (yield 69%).

DETD Oxidation of 1D-2-(1',2'-O-dipalmitoyl-sn-glycero-3'-phospho)-3,6-di-myo-inositol-4,5-bis(dibenzylphosphate) 51 by Procedure A was complete at r.t. in min; worked up and purification as in Example 1, gave 1D-2-(1',2'-O-dipalmitoyl-sn-glycero-3'-phospho)-3,6-di-1-myo-inosose-4,5-bis(dibenzylphosphate) (yield 86%).

DETD Oxidation of 1D-1-(1',2'-O-dipalmitoyl-sn-glycero-3'-phospho)-3,6-di-O-benzyl-myo-inositol-4,5-bis(dibenzylphosphate)-benzyl ester 49 using Procedure A, and purification as in the general protocol gave 1D-1-(1',2'-O-dipalmitoyl-sn-glycero-3'-phospho)-3,6-di-O-benzyl-2myo-inosose-4,5-bis(dibenzylphosphate)-benzyl ester 50 (yield 65%).



DETD Oxidation of 1D-2-(1',2'-O-dipalmitoyl-sn-glycero-3'-phospho)-3,6-di-O-benzyl-myo-inositol-4,5-bis(dibenzylphosphate)-benzyl ester 52 by Procedure A, work up and purification as in the general protocol gave 1D-2-(1',2'-O-dipalmitoyl-sn-glycero-3'-phospho)-3,6-di-O-benzyl-1-myo-inosose-4,5-bis(dibenzylphosphate)-benzyl ester 53 (yield 72%).

L84 ANSWER 4 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2000:174129 USPATFULL

TITLE: Preparation for the application of agents in mini-droplets

INVENTOR(S): Cevc, Gregor, Heimstetten, Germany, Federal Republic of

PATENT ASSIGNEE(S): Idea AG, Munich, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6165500		20001226
APPLICATION INFO.:	US 1992-844664		19920408 (7)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1990-4026834	19900824
	DE 1990-4026833	19900824
	DE 1991-4107153	19910306
	WO 1991-EP1596	19910822
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Kishore, Gollamudi S.	
LEGAL REPRESENTATIVE:	Davidson, Davidson & Kappel, LLC	
NUMBER OF CLAIMS:	35	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	31 Drawing Figure(s); 21 Drawing Page(s)	
LINE COUNT:	4336	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a preparation for the application of agents in the form of minuscule droplets of fluid, in particular provided with membrane-like structures consisting of one or several layers of amphiphilic molecules, or an amphiphilic carrier substance, in particular for transporting the agent into and through natural barriers such as skin and similar materials. The preparation contains a concentration of edge active substances which amounts to up to 99 mol-% of the agent concentration which is required for the induction of droplet solubilization. Such preparations are suitable, for example, for the non-invasive applications of antidiabetics, in particular of insulin. The invention, moreover, relates to the methods for the preparation of such formulations.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . K. (1989) Arzneim. Forsch./Drug Res. 39, 1487-1491). In the case of plants, improved penetration into or through the cuticle could reduce the drug concentration required for a given application and thus significantly diminish pollution problems (Price, C. E. (1981) In: The. . .

DETD . . . form of a cyclic lactone residue. The aldehyde- or keto-groups in a derivatised mono- or disaccharide residue can also be reduced to a hydroxy group, e.g. in inositol, sorbitol or D-mannitol; also, one or several hydroxy groups can be replaced by. . .

DETD . . . the form of cyclic lactone residues. The aldehyde- or keto-groups in a derivatised mono- or disaccharide residue, moreover, can be reduced to hydroxy groups, e.g. in inositol, sorbitol or D-mannitol. Furthermore, individual hydroxy groups can be replaced by hydrogen atoms, e.g.. . .

DETD A carbohydrate can result from a cleaving action, starting with one of the mentioned mono- or disaccharides, by a strong oxidation agent, such as periodic acid. Amongst the biologically most important or

most active carbohydrates are e.g. 2-acetamido-N-(epsilon-amino-caproyl)-2-deoxy-beta-glucopyranosylamine, 2-acetamido-2-amino-1,2-dideoxy-beta-glucopyranose, 2-acetamido-1-beta-(aspartamido)-1,2-dideoxyglucose, 2-acetamido-4,6-o-benzyliden-2-deoxybeta-glucopyranose, . . . . . beta-glucopyranoside, hesperidin, n-hexyl-beta-glucopyranoside, hyaluronic acid, 16-alpha-hydroxyestronglucuronide, 16-beta-hydroxyestron glucuronide, hydroxyethyl starch, hydroxypropylmethyl-cellulose, 8-hydroxyquinolin-beta-glucopyranoside, 8-hydroxyquinolin glucuronide, idose, (-)-idose, indole-3- lactic acid, indoxyl-beta-glucoside, epi-inositol, myo-inositol, myo-inositol bisphosphate, myo-inositol-1,2-cyl phosphate, scyllo-inositol, inositolhexaphosphate, inositolhexasulfate, myo-inositol 2-monophosphate, myo-inositol trisphosphate, (q)-epi-inosose-2, scyllo-inosose, inulin, isomaltose, isomaltotriose, isosorbid dinitrate, 11-ketoandrosterone beta-glucuronide, 2-ketogluconic acid, 5-ketogluconic acid, alpha-ketopropionic acid, lactal, lactic acid, lactitol, lactobionic acid, lacto-N-tetraose, . . . . . acid, neuraminic acid beta-methylglycoside, neuramine-lactose, nigeran, nigerantetrasaccharide, nigerose, n-nonyl glucoside, n-nonyl-beta-glucopyranoside, octadecylthio-ethyl 4-o-alpha-galactopyranosyl-beta-galactopyranoside, octadecylthioethyl 4-o-(4-o-[6-o-alpha-glucopyranosyl-alpha-glucopyranosyl]-alpha-glucopyranosyl)-beta-glucopyranoside, octanoyl n-methylglucamide, n-octyl alpha-glucopyranoside, n-octyl-beta-glucopyranoside, oxidised starch, pachyman, palatinose, panose, pentaerythritol, pentaerythritol diformal, 1,2,3,4,5-pentahydroxy, capronic acid, pentosanpolysulfate, perseitol, phenolphthalein glucuronic acid, phenolphthalein mono-beta-glucosiduron phenyl 2-acetamido-2-deoxy-alpha-galactopyranoside, phenyl2-acetamido-2-deoxy-alpha-glucopyranoside, . . . . .

DETD Oxidoreductases, such as: alcohol dehydrogenase (1.1.1.1), alcohol dehydrogenase (NADP dependent) (1.1.1.2), glycerol dehydrogenase (1.1.1.6), glycerophosphate dehydrogenase (1.1.1.8), xylulose reductase (1.1.1.10), polyol dehydrogenase (1.1.1.14), sorbitol dehydrogenase (1.1.1.14), myo-inositol dehydrogenase (1.1.1.18), uridine 5'-diphosphoglucose dehydrogenase (1.1.1.22), glyoxalate reductase (1.1.1.26), lactate dehydrogenase (1.1.1.27), lactate dehydrogenase (1.1.1.28), glycerate dehydrogenase (1.1.1.29), beta-hydroxybutyrate dehydrogenase (1.1.1.30), beta-hydroxyacyl CoA dehydrogenase (1.1.1.35), malate dehydrogenase (1.1.1.37), . . . . . glutamic dehydrogenase (1.4.1.3), glutamate dehydrogenase (NADP) (1.4.1.4), L-amino acid oxidase (1.4.3.2), D-amino acid oxidase (1.4.3.3), monoaminoxidase (1.4.3.4), diaminoxidase (1.4.3.6), dihydrofolate reductase (1.5.1.3), 5,10-methylenetetrahydrofolat dehydrogenase (1.5.1.5), saccharopine dehydrogenase NAD+ (1.5.1.7), octopine dehydrogenase (1.5.1.11), sarcosine oxidase (1.5.3.1), sarcosine dehydrogenase (1.5.99.1), glutathione reductase (1.6.4.2), ferridoxin-NADP+ reductase (1.6.7.1), NADPH-FMN oxidoreductase (1.6.99.1), cytochrome c reductase (1.6.99.3), NADH-fmn oxidoreductase (1.6.99.3), dihydropteridin reductase (1.6.99.7), uricase (1.7.3.3), diaphorase (1.8.1.4), lipoamide dehydrogenase (1.8.1.4), cytochrome oxidase (1.9.3.1), nitrate reductase (1.9.6.1), phenolase (1.10.3.1), ceruloplasmine (1.10.3.2), ascorbate oxidase (1.10.3.3), NADH peroxidase (1.11.1.1), catalase (1.11.1.6), lactoperoxidase (1.11.1.7), myeloperoxidase (1.11.1.7), peroxidase (1.11.1.7), glutathione. . . . . salicylate hydroxylase (1.14.13.7), p-hydroxybenzoate hydroxylase (1.14.13.2), luciferase (bacterial) (1.14.14.3), phenylalanine hydroxylase (1.14.16.1), dopamine-beta-hydroxylase (1.14.17.1), tyrosinase (1.14.18.1), superoxide dismutase (1.15.1.1), ferredoxine-NADP reductase (1.18.1.2), etc..

Transferases, such as: catecholic o-methyltransferase (2.1.1.6), phenylethanol-amine N-methyl-transferase (2.1.1.28), aspartate transcarbamylase (2.1.3.2), ornithine carbamyltransferase (2.1.3.3), transketolase (2.2.1.1), transaldolase. . . . .

DETD . . . cobra), *Naja Naja kaouthia*, *Mycoplasma gallisepticum*, *Perseu americana* (avocado), *Phaseolus coccineus* (beans), *Phaseolus limensis*, *Phaseolus lunatus*, *Phaseolus vulgaris*, *Phytolacca americana*, *Pseudomonas aeruginosa* PA-I, *Pisum sativum* (pea), *Ptilota plumosa* (red algae), *Psophocarpus tetragonolobus* (winged bean), *Ricinus communis* (castor bean), *Robinia pseudoacacia* (false. . .

DETD . . . be parts of a biological extract. As sources of biologically and/or pharmacologically active extracts, the following are worth-mentioning: for example, *Acetobacter pasteurianum*, *Acokanthera ouabaio cathel*, *Aesculus hippocastanum*, *Ammi visnaga* Lam., *Ampi Huasca*, *Apocynum Cannabium*, *Arthrobotrys superba* var. *oligospora* (ATCC 11572), *Atropa*. . .

DETD Next, the carrier composition or concentration is adapted by

reducing the edge activity in the system to an extent which

ensures the vesicle stability as well vesicle deformability to be. . .

DETD If the pore diameter is reduced to 0.05 micrometers only suspensions with L/S ratios below 2/1 can still be filtered.

L84 ANSWER 5 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2000:40863 USPATFULL

TITLE: Highly sensitive method for assaying chiro-inositol and compositions for the assay

INVENTOR(S): Kozuma, Takuji, Shizuoka, Japan

Takahashi, Mamoru, Shizuoka, Japan

PATENT ASSIGNEE(S): Asahi Kasei Kogyo Kabushiki Kaisha, Osaka, Japan  
(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6046018		20000404
	WO 9842863		19980110
APPLICATION INFO.:	US 1999-308575		19990608 (9)
	WO 1998-JP1215		19980320
			19990608 PCT 371 date
			19990608 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1997-72878	19970326
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Leary, Louise N.	
LEGAL REPRESENTATIVE:	Young & Thompson	
NUMBER OF CLAIMS:	5	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	6 Drawing Figure(s); 6 Drawing Page(s)	
LINE COUNT:	1012	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to an assay method of chiroinositol which comprises reacting a specimen containing chiroinositol with

1) a dehydrogenase, which catalyses at least reversible reaction with a substrate of chiroinositol in the presence of a coenzyme selected from NAD(P)s and a coenzyme selected from thio-NAD(P)s,

2) A1 and

3) B1

to form cycling reaction of the formula ##STR1## wherein a product is a compound, from which 2 or 4 hydrogen atoms are deleted from chiroinositol, A1 is NAD(P)s or thio-NAD(P)s, A2 is a reduced form of A1, B1 is a reduced form of NAD(P)s in case of A1 being thio-NAD(P)s or a reduced form of thio-NAD(P)s in case of A1 being NAD(P)s and B2 is an oxidized form of B1, and determining an amount of converted A2 or B1 by the said reaction, and a composition for assay of chiroinositol. Chiroinositol can be assayed by accurate,

simple, low price and high sensitive method.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . compound, from which 2 or 4 hydrogen atoms are deleted from chiroinositol, A1 is NAD(P)s or thio-NAD(P)s, A2 is a **reduced** form of A1, B1 is a **reduced** form of NAD(P)s in case of A1 being thio-NAD(P)s or a **reduced** form of thio-NAD(P)s in case of A1 being NAD(P)s and B2 is an oxidized form of B1, and determining an. . .

SUMM . . . compound, from which 2 or 4 hydrogen atoms are deleted from chiroinositol, A1 is NAD(P)s or thio-NAD(P)s, A2 is a **reduced** form of A1, B1 is a **reduced** form of NAD(P)s in case of A1 being thio-NAD(P)s or a **reduced** form of thio-NAD(P)s in case of A1 being NAD(P)s and B2 is an oxidized form of B1, and determining an. . .

SUMM 3) in the above 2), at least a coenzyme selected from **reduced** thio-NAD (P)s in case of at least a coenzyme selected from NAD(P)s, or in the above 2), at least a coenzyme selected from **reduced** NAD(P)s in case of at least ,t coenzyme selected from thio-NAD(P)s.

SUMM . . . in body fluid such as blood or urine for diagnosis of diabetes mellitus, especially insulin resistance, is useful, and suggest reduction/oxidation analysis using enzyme, however no concrete method has proposed.

SUMM In order to assay trace amount of chiroinositol in vivo in clinical biochemical test, not only direct assay method of **reduced** coenzyme using dehydrogenase but also a combination with coloring agent for assay is resulted to insufficient sensitivity. We have found. . . dehydrogenase derived from Aerobacter aerogenes acts on myoinositol in the presence of NAD to delete 2 hydrogen atoms to form myoinosose 2, under sufficient progressive condition for reaction, a compound generated from a reaction in which at first 2 hydrogen atoms. . . not detected by paper chromatography [J. Biol. Chem., 241 (4); 1966, 800-806]. Since the said final compound is different from myoinosose 2 and is very unstable, to construct a stable enzymatic cycling reaction might be impossible.

SUMM . . . compound, from which 2 or 4 hydrogen atoms are deleted from chiroinisitol, A1 is NAD(P)s or thio-NAD(P)s, A2 is a **reduced** form of A1, B1 is a **reduced** form of NAD(P)s in case of A1 being thio-NAD(P)s or a **reduced** form of thio-NAD(P)s in case of A1 being NAD(P)s and B2 is an oxidized form of B1, and can be. . .

SUMM . . . compound, from which 2 or 4 hydrogen atoms are deleted from chiroinositol, A1 is NAD(P)s or thio-NAD(P)s, A2 is a **reduced** form of A1, B1 is a **reduced** form of NAD(P)s in case of A1 being thio-NAD (P)s or a **reduced** form of thio-NAD(P)s in case of A1 being NAD(P)s and B2 is an oxidized form of B1, and determining an. . .

SUMM 3) in the above 2), at least a coenzyme selected from **reduced** thio-NAD(P)s in case of at least a coenzyme selected from NAD(P)s, or in the above 2), at least a coenzyme selected from **reduced** NAD(P)s in case of at least a coenzyme selected from thio-NAD(P)s.

SUMM . . . production (detected by lead acetate paper) -  
 Acetoin production (K.sub.2 HPO.sub.4) -  
 Acetoin Production (NaCl) -  
 MR test -  
 Nitrate **reduction** test (gas formation) -  
 (NO.sub.2 - detection) -  
 (NO.sub.3 - detection) +  
 Utilization on Simmons medium  
 Citrate -  
 Malate -

SUMM . . . C. + + +  
 55.degree. C. + + +  
 60.degree. C. ND ND -  
 70.degree. C. - - +  
 Nitrate **reduction** d + -  
 GC mole % of DNA 44.5 46.4 41.9

(Type) (Type)

44.3.about.50.3 42.9.about.49.9

- SUMM The present enzyme catalyses a reaction for generating **reduced** coenzyme [NAD(P)Hs and thio-NAD(P)Hs] in the presence of chiroinositol and coenzyme [NAD(P)s and thio-NAD(P)s]. Examples of the above NAD(P)s are. . .
- SUMM . . . and deamino NAD; 14 U/ml) 20 .mu.l is added and stirred. Absorption changes per minute in specific wavelength for each **reduced** coenzyme is measured to obtain initial reaction rate. (For NAD and deamino NAD, measured value is increased number by ten. .
- SUMM A product in the present cycling reaction is an amount of **reduced** NAD generated by the reaction with chiroinositol and excess amount of NAD. In the reaction, 2 hydrogen atoms are deleted. . the first reaction and 2 hydrogen atoms are further deleted at the second reaction. These are confirmed by increase in **reduced** NAD, which is determined by an amount of formazan pigment having maximum absorption at 550 nm generated as a result of an act on of NBT (nitroblue tetrazolium) on the **reduced** NAD in the presence of diaphorase.

SUMM TABLE 1

Substrate	Relative activity
chiroinositol	100%
myoinositol	9%
scylloinositol	0%
epi-inositol	0%
galactose	0%
fructose	0%
mannose	0%
mannitol	0%

SUMM TABLE 3

	A.r.1215 origin	S.r.301 origin
chiroinositol	100%	100%
myoinositol	33% 0%	
scylloinositol	0% 0%	
epi-inositol	0% 4%	
fructose	0% 0%	
mannose	10% 0%	
mannitol	0% 0%	

- SUMM . . . 2 or 4 hydrogen atoms are deleted from chiroinositol, A1 and B2 are NAD(P)s or thio-NAD(P)s, A1 and B1 are **reduced** form thereof, and in A1 and B1, when A1 is thio-NAD(P)s, B1 is NAD(P)Hs, and when B1 is thio-NAD(P)H, A1. . .
- SUMM In case of enzyme cycling method in the present invention, if A1 and B1 are expensive, in order to **reduce** amount of A1 and B1, a combination of a dehydrogenase which constitutes a reaction of B2.fwdarw.B1 and not reacted with. . . dehydrogenase which constitutes a reaction of A2.fwdarw.A1 and not reacted with chiroinositol and substrate for dehydrogenase can be used for **reducing** amount of A1 and B1.
- SUMM **Reduced** coenzyme assay by measuring absorption change used in the present invention can be performed by other known method.
- DETD As shown in the above, the present invention provide rate assay of the **reduced** coenzyme and the blank assay for the specimen can be ommitted. Consequently, simple.assay can be performed, and sensitivity of. . .
- CLM What is claimed is:  
. . . compound, from which 2 or 4 hydrogen atoms are deleted from chiroinositol, A1 is NAD(P)s or thio-NAD(P)s, A2 is a **reduced**

form of A1, B1 is a **reduced** form of NAD(P)s in case of A1 being thio-NAD(P)s or a **reduced** form of thio-NAD(P)s in case of A1 being NAD(P)s and B2 is an oxidized form of B1, and determining an. . .

. . . least a coenzyme selected from NAD(P)s and thio-NAD(P)s, and 3) in the above 2), at least a coenzyme selected from **reduced** thio-NAD(P)s in case of at least a coenzyme selected from NAD(P)s, or in the above 2), at least a coenzyme selected from **reduced** NAD(P)s in case of at least a coenzyme selected from thio-NAD(P)s.

L84 ANSWER 6 OF 10 USPATFULL on STN

ACCESSION NUMBER: 94:90948 USPATFULL  
 TITLE: Highly sensitive assay method for myo-inositol, composition for practicing same, novel myo-inositol dehydrogenase, and process for producing same  
 INVENTOR(S): Ueda, Shigeru, Shizuoka, Japan  
 Takahashi, Mamoru, Shizuoka, Japan  
 Misaki, Hideo, Shizuoka, Japan  
 Imamura, Shigeyuki, Shizuoka, Japan  
 Matsuura, Kazuo, Shizuoka, Japan  
 PATENT ASSIGNEE(S): Asahi Kasei Kogyo Kabushiki Kaisha, Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5356790		19941018
APPLICATION INFO.:	US 1993-106693		19930816 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1991-761465, filed on 18 Sep 1991, now abandoned		

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1990-2249775	19900918
	JP 1990-2249776	19900918
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Wityshyn, Michael G.	
ASSISTANT EXAMINER:	Leary, Louise N.	
LEGAL REPRESENTATIVE:	Young & Thompson	
NUMBER OF CLAIMS:	5	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 8 Drawing Page(s)	
LINE COUNT:	819	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Myo-inositol in a specimen is assayed by reacting a specimen containing myo-inositol with:

a) myo-inositol dehydrogenase using a thio-NADP group or thio-NAD group and an NADP group or NAD group as coenzymes, and which catalyzes a reversible reaction forming myo-inosose from myo-inositol,

b ) A.sub.1 and

c) B.sub.1

to effect a cycling reaction ##STR1## wherein A.sub.1 is a thio-NADP group, thio-NAD group, NADP group or NAD group, A.sub.2 is a reduced form of A.sub.1, when A.sub.1 is a thio-NADP group or thio-NAD group, B.sub.1 is a reduced NADP group or reduced NAD group and when A.sub.1 is an NADP group or NAD group, B.sub.1 is a reduced thio-NADP group or reduced thio-NAD group, and wherein B.sub.2 is an oxidized form of B.sub.1. The change in the amount of A.sub.2 generated or B.sub.1 consumed by the cycling reaction is measured to perform the assay. A composition for performing the assay comprises the above myo-inositol dehydrogenase, as well as the above components A.sub.1 and B.sub.1. The

myo-inositol dehydrogenase can be produced by culturing a suitable microorganism belonging to genus *Bacillus*, particularly *Bacillus* sp. No. 3 FERM BP-3013.

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB a) myo-inositol dehydrogenase using a thio-NADP group or thio-NAD group and an NADP group or NAD group as coenzymes, and which catalyzes a reversible reaction forming myo-inosose from myo-inositol,

SUMM (1) myo-inositol dehydrogenase using one of coenzymes of thionicotinamide adonine dinucleotide phosphate group (hereinafter designated thio-NADP group) or thionicotinamide adenine dinucleotide group. . . (hereinafter designated NADP group) or nicotinamide adonine dinucleotide group (hereinafter designated NAD group) and which catalyzes a reversible reaction forming myo-inosose from a substrate of myo-inositol,

DETD *Aerobacter aerogenes* (J. Biol. Chem., 241, 800-806 (1966)); *Klebsiella pneumoniae*, *Serratia marcescens*, *Cryptococcus melibiosum* (Biochim. Biophys. Acta., 293, 295-303 (1973)); and bovine brain (Biochem. Biophys. Res. Comm., 68, 1133-1138 (1976)); *Bacillus*. . .

DETD Among these, *Aerobacter aerogenes*, *Klebsiella pneumoniae* and *Serratia marcescens* are known as etiologic microorganisms for pneumonia and opportunistic infections (Standard Microbiology, 2nd edn., pp. 209-212, Igaku Shoin Publishing. . .

DETD The enzyme catalyzes essentially a reaction of myo-inositol and NAD to generate myo-inosose and reduced NADH, as follows:

DETD myo-inositol+NAD.about.myo-inosose  
\*+reduced NADH \*(2,4,6/3,5-pentahydroxy cyclohexanone)

DETD Glyoxylate dehydrogenase (EC.1.2.1.17) (*Pseudomonas oxalaticus*) and CoA and glyoxylate,

DETD Benzaldehyde dehydrogenase (EC.1.2.1.7) (*Pseudomonas fluorescens*) and benzaldehyde.

CLM What is claimed is:

1. A method of assaying myo-inositol comprising reacting a specimen containing myo-inositol with the following reagents: a) myo-inositol dehydrogenase which, in the presence of a thionicotinamide adenine dinucleotide group (thio-NAD-group) and a nicotinamide adenine dinucleotide group (NAD group) as coenzymes, catalyzes a reversible reaction forming myo-inosose from myo-inositol, b) A.sub.1 and c) B.sub.1 ; to effect a cycling reaction ##STR5## wherein A.sub.1 is a thio-NAD group or NAD. . . NAD group and when A.sub.1 is an NAD group, B.sub.1 is a reduced thio-NAD group, and wherein B.sub.2 is an oxidized form of B.sub.1 ; and measuring a change in the amount of A.sub.2 generated or B.sub.1 consumed by the cycling reaction wherein A.sub.1 and B.sub.1 are each used at a concentration of 0.02-100 mM, and wherein said myo-inositol dehydrogenase is used at a concentration of 5-1000 U/ml.

3. A reagent composition for assaying myo-inositol, comprising: a) myo-inositol dehydrogenase which, in the presence of a thionicotinamide adenine dinucleotide group (thio-NAD group) and a nicotinamide adenine dinucleotide group (NAD group) as coenzymes, catalyzes a reversible reaction forming myo-inosose from myo-inositol, b) A.sub.1 and c) B.sub.1 ; wherein A.sub.1 is a thio-NAD group or NAD group, when A.sub.1 is a thio-NAD. . . of a thio-NAD group wherein A.sub.1 and B.sub.1 are each present in a concentration of 0.02-100 mM, and wherein said myo-inositol dehydrogenase is present in a concentration of 5-1000 U/ml.

4. Myo-inositol dehydrogenase having the following properties: substrate specificity for myo-inositol and catalyzes a reaction myo-inositol+NAD.about.myo-inosose+reduced NADH, said myo-inositol dehydrogenase having the following physicochemical properties: (1)

molecular weight: 130,000.+-15,000 (gel filtration method by TSK gel G 3000 SW) (2) iso-electric point: pH 4.5.+-0.5 (3) Km-value: Km value for myo-inositol: 0.64 mM Km value for NAD: 0.004 mM  
(4) optimum pH: approximately ph. 9.5 (5) pH-stability: more than 80% retained.

L84 ANSWER 7 OF 10 USPATFULL on STN

ACCESSION NUMBER: 93:57049 USPATFULL  
TITLE: 3-deoxy-3-substituted analogs of phosphatidylinositol  
INVENTOR(S): Kozikowski, Alan P., Ponte Verde Beach, FL, United States  
Tuckmantel, Werner, Jacksonville, FL, United States  
Faug, Abdul H., Jacksonville, FL, United States  
Powis, Garth, Tucson, AZ, United States  
PATENT ASSIGNEE(S): Mayo Foundation for Medical Education and Research, Rochester, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5227508		19930713
APPLICATION INFO.:	US 1992-825523		19920124 (7)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Ramsuer, Robert W.		
ASSISTANT EXAMINER:	Ambrose, Michael G.		
LEGAL REPRESENTATIVE:	Merchant, Gould, Smith, Edell, Welter & Schmidt		
NUMBER OF CLAIMS:	15		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	6 Drawing Figure(s); 6 Drawing Page(s)		
LINE COUNT:	927		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides 3-deoxy-3-substituted analogs of phosphatidylinositol which are useful to inhibit the growth of mammalian cells, i.e., to treat neoplastic conditions and other proliferative disorders of mammalian cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD The key intermediate, 2,4,5,6-tetra-O-benzyl-3-deoxy-3-fluoro-D-myo-inositol (40), is available as outlined earlier.  
Inversion of the stereochemistry at C-1 is brought about by oxidation to the inosose ((COCl).sub.2, DMSO, i-Pr.sub.2 NEt), followed by stereoselective reduction of the 1-ketone with L-Selectride.RTM. (Aldrich Chem. Co.). The resulting axial alcohol.

L84 ANSWER 8 OF 10 USPATFULL on STN

ACCESSION NUMBER: 76:52995 USPATFULL  
TITLE: Process for preparing aminocyclitol antibiotics  
INVENTOR(S): Daum, Sol J., Albany, NY, United States  
Clarke, Robert L., Bethlehem, NY, United States  
PATENT ASSIGNEE(S): Sterling Drug Inc., New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3982996		19760928
APPLICATION INFO.:	US 1975-615593		19750922 (5)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Tanenholtz, Alvin E.		
LEGAL REPRESENTATIVE:	Webb, William G., Wyatt, B. W.		
NUMBER OF CLAIMS:	12		
EXEMPLARY CLAIM:	1		
LINE COUNT:	728		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Aminocyclitol antibiotics of the streptamine, deoxystreptamine or dideoxystreptamine type are prepared by culturing a nutrient medium



containing carbohydrates, a source of assimilable nitrogen, essential salts and a non-nitrogen containing cyclitol with a mutant of an aminocyclitol antibiotic producing organism.

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM Yet a process that would permit the use of cyclitols, instead of aminocyclitols, for incorporation into aminocyclitol-type antibiotics by microorganism mutants using the Rinehart/Shier method would provide a very significant advance in the aminocyclitol antibiotic art, because the method would afford, by judicious selection of the microorganism and the cyclitol subunit, a certain degree of biogenetic "tailoring" of the resultant antibiotic molecule. Moreover, since the aminocyclitols are. . . products could be realized. (For example, streptomycin, at present prices, costs about \$1 per gram, whereas its probable biogenetic precursor, scyllo-inosose, can be obtained in about 80% yield by fermentative oxydation of myo-inositol, which only costs about 2 cents per gram at present).

DETD . . . [dl-1,2,3,4,5-cyclohexanepentol (1,2,4-cis)] [McCasland et al., J. Am. Chem. Soc. 75, 4020 (1953)] (0.40 mole) was subjected to microbiological oxidation by Acetobacter suboxydans using the procedure described by Posternak, Helv. Chim. Acta 33, 1594-1596 (1950). To the resulting broth was added 5. . .

DETD The latter was subjected to microbiological oxidation by Acetobacter suboxydans using the procedure described by Posternak recorded above in Preparation 1, and the product was isolated as described in. . .

=> d ibib abs 9

L84 ANSWER 9 OF 10 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN  
 ACCESSION NUMBER: 97:313486 SCISEARCH  
 THE GENUINE ARTICLE: WT993  
 TITLE: Reactions of the ketone derived from (+/-)-3,4,5-tri-O-benzyl-1,2-O-isopropylidene-myo-inositol: Preparation of racemic derivatives of epi-inositol and of 4-C-methyl-epi-[(+/-)-iso-laminitol] and 4-C-methyl-myo-inositol [(+/-)-laminitol]  
 AUTHOR: Gigg J; Gigg R (Reprint)  
 CORPORATE SOURCE: NATL INST MED RES, DIV LIPID & GEN CHEM, MILL HILL, LONDON NW7 1AA, ENGLAND (Reprint); NATL INST MED RES, DIV LIPID & GEN CHEM, LONDON NW7 1AA, ENGLAND  
 COUNTRY OF AUTHOR: ENGLAND  
 SOURCE: CARBOHYDRATE RESEARCH, (26 MAR 1997) Vol. 299, No. 1-2, pp. 77-83.  
 Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, OXON, ENGLAND OX5 1GB.  
 ISSN: 0008-6215.  
 DOCUMENT TYPE: Article; Journal  
 FILE SEGMENT: PHYS; LIFE; AGRI  
 LANGUAGE: English  
 REFERENCE COUNT: 27

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Oxidation of (+/-)-3,4,5-tri-O-benzyl-1,2-O-isopropylidene-myo-inositol with the pyridine-SO<sub>3</sub> complex in methyl sulfoxide gave the ketone which was reduced with sodium borohydride to give almost exclusively the corresponding epi-inositol derivative. Reaction of the ketone with diazomethane gave an epoxide which was reduced with lithium aluminium hydride to give a 4-C-methyl-myo-inositol derivative and reaction of the ketone with methyl magnesium iodide gave the isomeric 4-C-methyl-epi-inositol derivative. (C) 1997 Elsevier Science Ltd.

=> d ibib abs 10

L84 ANSWER 10 OF 10 WPIX COPYRIGHT 2003 THOMSON DERWENT on STN  
 ACCESSION NUMBER: 2002-158901 [21] WPIX  
 DOC. NO. CPI: C2002-049937  
 TITLE: L-*epi*-Inositol derivative is useful  
 as an intermediate of medicaments or agrochemicals.  
 DERWENT CLASS: B05 C03  
 PATENT ASSIGNEE(S): (HOKK) HOKKO CHEM IND CO LTD  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 2001335544	A	20011204	(200221)*		22

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 2001335544	A	JP 2000-158238	20000529

PRIORITY APPLN. INFO: JP 2000-158238 20000529

AN 2002-158901 [21] WPIX

AB JP2001335544 A UPAB: 20020403

NOVELTY - A L-*epi*-inositol derivative or its salt (I),  
 are new.

DETAILED DESCRIPTION - A L-*epi*-inositol  
 derivative of formula (I) or its salt, are new.

R1, R4-R7 = H, acyl or alkyl;

when R2 = amino, acylamide, alkylamino or N-acyl-N-alkylamino, R3 H;  
 when R2 = hydroxyl or acyloxyl, R3 = hydroxymethyl, acyloxymethyl,  
 azidemethyl, aminomethyl, acylamidemethyl, N-alkylaminomethyl or  
 N-acyl-N-alkylaminomethyl; when R2 = O, R3 methylene, R3 + R2 +  
 spirocarbon at the second position of the cyclohexane ring bind to each  
 other to form 2,21-anhydro-2-C-hydroxymethyl of spiroepoxy ring.

INDEPENDENT CLAIMS are also included for a method of preparing  
 2-amino-2-deoxy-L-*epi*-inositol of formula (II) which  
 comprises allowing the ketone group of L-*epi*-2-  
 inosose of formula (III) to react with an ammonia derivative for  
 dehydration condensation, and reducing with a reducing agent in the  
 presence of a catalyst to convert into an amino group.

USE - The inositol derivative is useful as an intermediate of  
 medicaments or agrochemicals.

ADVANTAGE - The inositol derivative having biological activity is  
 inexpensively prepared in high yields.

Dwg.0/0

MARX 09/980,453

=&gt; d his

(FILE 'HOME' ENTERED AT 14:25:34 ON 18 AUG 2003)

FILE 'CAPLUS' ENTERED AT 14:26:20 ON 18 AUG 2003

L1 65 S KANBE K?/AU  
 L2 4489 S TAKAHASHI A?/AU  
 L3 8664 S MORI T?/AU  
 L4 457 S TAMAMURA T?/AU  
 L5 6978 S TAKEUCHI T?/AU  
 L6 1234 S KITA Y?/AU  
 L7 21776 S L1-6  
 L8 3 S L7 AND EPI-INOSITOL  
 L9 7 S L7 AND ?INOSOSE  
 L10 7 S L8-9  
 SELECT RN L10 1-7

FILE 'REGISTRY' ENTERED AT 14:29:26 ON 18 AUG 2003

L11 36 S E1-36

FILE 'CAPLUS' ENTERED AT 14:29:32 ON 18 AUG 2003

L12 7 S L10 AND L11 *7 cites of 36 cpts displayed*

FILE 'CAPLUS' ENTERED AT 14:29:54 ON 18 AUG 2003

=&gt; d ibib abs hitstr ind 1-7

L12 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:266870 CAPLUS

DOCUMENT NUMBER: 138:270409

TITLE: Scyllo-inosose and scyllo-inositol  
manufactureINVENTOR(S): Kamibe, Kenji; Takahashi, Atsushi;  
Kita, Yuichi; Yamaguchi, Masanori;  
Tamamura, Takeshi; Mori, Tetsuya

PATENT ASSIGNEE(S): Hokko Chemical Industry Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003102492	A2	20030408	JP 2002-184912	20020625
PRIORITY APPLN. INFO.:		JP 2001-191161 A 20010625		

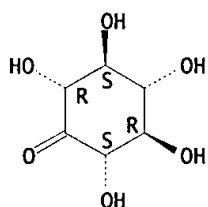
AB The scyllo-inosose is manufd. from myo-inositol with Pseudomonas and Acetobacter. The scyllo-inosose is reduced with an reductant such as sodium borohydride to get scyllo-inositol. The physiol. and morphol. characteristics of these microorganisms were given. The scyllo-inosose is an useful intermediate for manufg. pharmaceuticals. The scyllo-inositol is useful for control of. Alzheimer disease and for prepd. liq. crystal.

IT 488-64-2P, scyllo-Inosose  
 RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (scyllo-inosose and scyllo-inositol manuf.)

RN 488-64-2 CAPLUS

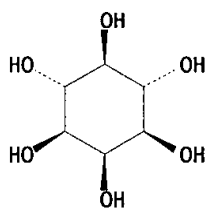
CN myo-2-Inosose (7CI, 9CI) (CA INDEX NAME)

Relative stereochemistry.

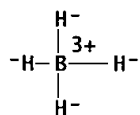


IT 87-89-8, myo-Inositol  
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)  
(scyllo-inosose and scyllo-inositol manuf.)  
RN 87-89-8 CAPLUS  
CN myo-Inositol (9CI) (CA INDEX NAME)

Relative stereochemistry.

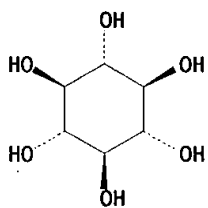


IT	16940-66-2, Sodium borohydride
	RL: RCT (Reactant); RACT (Reactant or reagent)
	(scyllo-inosose and scyllo-inositol manuf.)
RN	16940-66-2 CAPLUS
CN	Borate(1-), tetrahydro-, sodium (8CI, 9CI) (CA INDEX NAME)

 $\text{Na}^+$ 

IT 488-59-5P, scyllo-Inositol  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(scyllo-inosose and scyllo-inositol manuf.)  
RN 488-59-5. CAPLUS  
CN scyllo-Inositol (9CI) (CA INDEX NAME)

Relative stereochemistry.

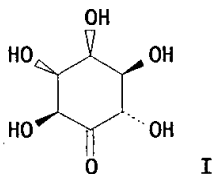


IC ICM C12P007-26  
 ICS C07C029-143; C07C035-16; C12N001-20; C12P007-18; C12R001-38;  
 C12R001-02  
 CC 16-2 (Fermentation and Bioindustrial Chemistry)  
 Section cross-reference(s): 1  
 ST scyllo inosose manuf myoinositol Pseudomonas Acetobacter; redn  
 scyllo inositol Alzheimer disease pharmaceutical  
 IT Acetobacter  
 Alzheimer's disease  
 Fermentation  
 Liquid crystals  
 Pseudomonas  
 Reducing agents  
 (scyllo-inosose and scyllo-inositol manuf.)  
 IT 488-64-2P, scyllo-Inosose  
 RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL  
 (Biological study); PREP (Preparation); USES (Uses)  
 (scyllo-inosose and scyllo-inositol manuf.)  
 IT 87-89-8, myo-Inositol  
 RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological  
 study); RACT (Reactant or reagent)  
 (scyllo-inosose and scyllo-inositol manuf.)  
 IT 16940-66-2, Sodium borohydride  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (scyllo-inosose and scyllo-inositol manuf.)  
 IT 488-59-5P, scyllo-Inositol  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)  
 (scyllo-inosose and scyllo-inositol manuf.)

L12 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN  
 ACCESSION NUMBER: 2002:672204 CAPLUS  
 DOCUMENT NUMBER: 137:200353  
 TITLE: D-allo-5-inosose, its microbial manufacture,  
 and manufacture of allo-inositol, D-allo-3-  
 inosose, or D-chiro-inositol  
 INVENTOR(S): Takahashi, Atsushi; Yamaguchi, Masanori;  
 Mori, Tetsuya; Kamibe, Kenji; Kita,  
 Yuichi; Tomoda, Akihiro; Tamamura,  
 Takeshi  
 PATENT ASSIGNEE(S): Hokko Chemical Industry Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 27 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002249459	A2	20020906	JP 2001-46412	20010222
PRIORITY APPLN. INFO.:			JP 2001-46412	20010222
OTHER SOURCE(S):			CASREACT 137:200353	

GI



AB D-Allo-5-inosose (I), useful as a starting material for manuf.

of pharmaceuticals, is manufd. by treatment of epi-  
 inositol (II) with microorganisms capable of oxidizing II into I.  
 Allo-inositol (III) is manufd. by redn. of I with alkali metal  
 borohydrides, alkali metal trialkoxyborohydrides, or alkali metal  
 cyanoborohydrides as reducing agents in aq. media and sepn. of III from  
 II. D-Allo-3-inosose (IV) is manufd. by treatment of III with  
 microorganisms capable of oxidizing III into IV. D-Chiro-inositol (V),  
 useful for treatment of non-insulin-dependent diabetes mellitus and  
 polycystic ovary syndrome, is manufd. by redn. of IV with alkali metal  
 borohydrides, alkali metal trialkoxyborohydrides, or alkali metal  
 cyanoborohydrides in aq. media and sepn. of V from III. V was manufd.  
 from II and purified in a total yield of 32.3%.

IT 643-10-7P, allo-Inositol

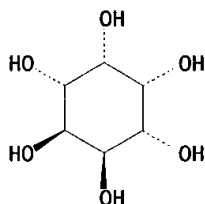
RL: BCP (Biochemical process); BMF (Bioindustrial manufacture); IMF  
 (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant);  
 BIOL (Biological study); PREP (Preparation); PROC (Process); RACT  
 (Reactant or reagent)

(manuf. of D-allo-5-inosose, allo-inositol, D-allo-3-  
 inosose, and D-chiro-inositol for pharmaceuticals)

RN 643-10-7 CAPLUS

CN allo-Inositol (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 488-58-4, epi-Inositol

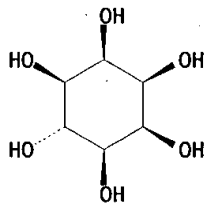
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);  
 PROC (Process); RACT (Reactant or reagent)

(manuf. of D-allo-5-inosose, allo-inositol, D-allo-3-  
 inosose, and D-chiro-inositol for pharmaceuticals)

RN 488-58-4 CAPLUS

CN epi-Inositol (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 643-12-9P, D-chiro-Inositol

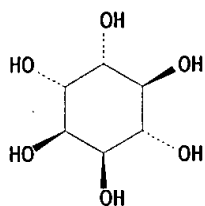
RL: BMF (Bioindustrial manufacture); IMF (Industrial manufacture); PUR  
 (Purification or recovery); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)

(manuf. of D-allo-5-inosose, allo-inositol, D-allo-3-  
 inosose, and D-chiro-inositol for pharmaceuticals)

RN 643-12-9 CAPLUS

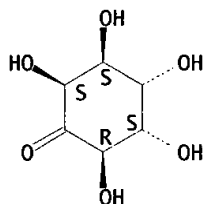
CN D-chiro-Inositol (9CI) (CA INDEX NAME)

Absolute stereochemistry.



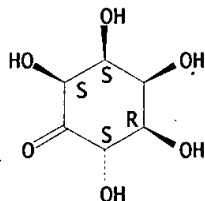
IT 148218-11-5P, D-Allo-3-Inosose 452335-59-0P,  
 D-allo-5-Inosose  
 RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); RCT  
 (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or  
 reagent)  
 (manuf. of D-allo-5-inosose, allo-inositol, D-allo-3-  
 inosose, and D-chiro-inositol for pharmaceuticals)  
 RN 148218-11-5 CAPLUS  
 CN D-allo-3-Inosose (9CI) (CA INDEX NAME)

Absolute stereochemistry.

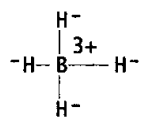


RN 452335-59-0 CAPLUS  
 CN D-allo-5-Inosose (9CI) (CA INDEX NAME)

Absolute stereochemistry.

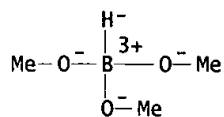


IT 13762-51-1, Potassium borohydride 16940-17-3, Sodium  
 trimethoxyborohydride 16940-66-2, Sodium borohydride  
 16949-15-8, Lithium borohydride 25895-60-7, Sodium  
 cyanoborohydride  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reducing agent; manuf. of D-allo-5-inosose, allo-inositol,  
 D-allo-3-inosose, and D-chiro-inositol for pharmaceuticals)  
 RN 13762-51-1 CAPLUS  
 CN Borate(1-), tetrahydro-, potassium (8CI, 9CI) (CA INDEX NAME)

K<sup>+</sup>

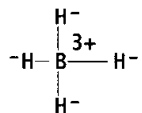
RN 16940-17-3 CAPLUS

CN Borate(1-), hydrotrimethoxy-, sodium, (T-4)- (9CI) (CA INDEX NAME)

● Na<sup>+</sup>

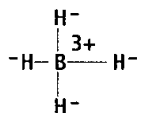
RN 16940-66-2 CAPLUS

CN Borate(1-), tetrahydro-, sodium (8CI, 9CI) (CA INDEX NAME)

Na<sup>+</sup>

RN 16949-15-8 CAPLUS

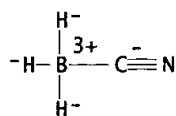
CN Borate(1-), tetrahydro-, lithium (8CI, 9CI) (CA INDEX NAME)

Li<sup>+</sup>

RN 25895-60-7 CAPLUS

CN Borate(1-), (cyano-.kappa.C)trihydro-, sodium, (T-4)- (9CI) (CA INDEX NAME)



● Na<sup>+</sup>

- IC ICM C07C049-497  
ICS C07C029-143; C07C035-16; C12P007-02; C12P007-26; C12R001-64;  
C12R001-01; C12R001-38
- CC 16-2 (Fermentation and Bioindustrial Chemistry)  
Section cross-reference(s): 63
- ST inosose inositol manuf fermn antidiabetic; polycystic ovary  
syndrome treatment inositol manuf; biochem oxidn redn inosose  
inositol manuf
- IT Oxidation  
(biol.; manuf. of D-allo-5-inosose, allo-inositol, D-allo-3-  
inosose, and D-chiro-inositol for pharmaceuticals)
- IT Acetobacter  
Agrobacterium  
Antidiabetic agents  
Enterobacter  
Fermentation  
Gluconobacter  
Haemophilus  
Pasteurella  
Pseudomonas  
Reducing agents  
Reduction  
Serratia  
Sphingomonas  
Xanthomonas  
Yersinia  
(manuf. of D-allo-5-inosose, allo-inositol, D-allo-3-  
inosose, and D-chiro-inositol for pharmaceuticals)
- IT Diabetes mellitus  
(non-insulin-dependent, therapeutic agents; manuf. of D-allo-5-  
inosose, allo-inositol, D-allo-3-inosose, and  
D-chiro-inositol for pharmaceuticals)
- IT Ovary, disease  
(polycystic, therapeutic agents; manuf. of D-allo-5-inosose,  
allo-inositol, D-allo-3-inosose, and D-chiro-inositol for  
pharmaceuticals)
- IT 643-10-7P, allo-Inositol  
RL: BCP (Biochemical process); BMF (Bioindustrial manufacture); IMF  
(Industrial manufacture); PUR (Purification or recovery); RCT (Reactant);  
BIOL (Biological study); PREP (Preparation); PROC (Process); RACT  
(Reactant or reagent)  
(manuf. of D-allo-5-inosose, allo-inositol, D-allo-3-  
inosose, and D-chiro-inositol for pharmaceuticals)
- IT 488-58-4, epi-Inositol  
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);  
PROC (Process); RACT (Reactant or reagent)  
(manuf. of D-allo-5-inosose, allo-inositol, D-allo-3-  
inosose, and D-chiro-inositol for pharmaceuticals)
- IT 643-12-9P, D-chiro-Inositol  
RL: BMF (Bioindustrial manufacture); IMF (Industrial manufacture); PUR  
(Purification or recovery); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); USES (Uses)  
(manuf. of D-allo-5-inosose, allo-inositol, D-allo-3-  
inosose, and D-chiro-inositol for pharmaceuticals)
- IT 148218-11-5P, D-Allo-3-Inosose 452335-59-0P,

**D-allo-5-Inosose**

RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(manuf. of D-allo-5-inosose, allo-inositol, D-allo-3-inosose, and D-chiro-inositol for pharmaceuticals)

IT 13762-51-1, Potassium borohydride 16940-17-3, Sodium trimethoxyborohydride 16940-66-2, Sodium borohydride 16949-15-8, Lithium borohydride 25895-60-7, Sodium cyanoborohydride

RL: RCT (Reactant); RACT (Reactant or reagent)  
(reducing agent; manuf. of D-allo-5-inosose, allo-inositol, D-allo-3-inosose, and D-chiro-inositol for pharmaceuticals)

L12 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:19320 CAPLUS

DOCUMENT NUMBER: 136:68818

TITLE: Microbial manufacture of L-chiro-1-inosose

INVENTOR(S): Takahashi, Atsushi; Kamibe, Kenji;  
Kita, Yuichi; Mori, Tetsuya;  
Yamaguchi, Masanori; Tomoda, Akihiro; Tamamura, Takeshi

PATENT ASSIGNEE(S): Hokko Chemical Industry Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002000285	A2	20020108	JP 2000-186337	20000621
PRIORITY APPLN. INFO.:			JP 2000-186337	20000621

OTHER SOURCE(S): CASREACT 136:68818

AB L-Chiro-1-inosose (I), useful as an enzyme inhibitor or an intermediate for pharmaceuticals, is manufd. with microorganisms from myo-inositol (II). Xanthomonas sp. AB10198 (FERM P-17893) was cultured in a liq. medium contg. II at 27.degree. for 5 days to give I at 141 mg/mL in 95% conversion.

IT 87-89-8, myo-Inositol

RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);

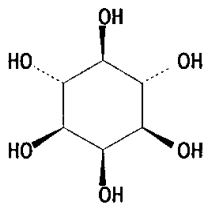
PROC (Process); RACT (Reactant or reagent)

(microbial manuf. of chiro-inosose from myo-inositol)

RN 87-89-8 CAPLUS

CN myo-Inositol (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 56816-02-5P, L-chiro-1-Inosose

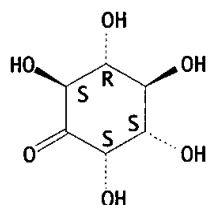
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)

(microbial manuf. of chiro-inosose from myo-inositol)

RN 56816-02-5 CAPLUS

CN L-chiro-1-Inosose (9CI) (CA INDEX NAME)

Absolute stereochemistry.

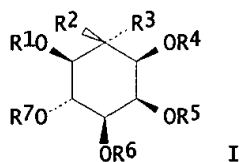


IC ICM C12P007-26  
 ICS C12N001-20; C12P007-18; C12P007-26; C12R001-64; C12R001-01;  
 C12R001-38; C12R001-02; C12R001-18; C12R001-425; C12R001-185;  
 C12R001-21  
 CC 16-5 (Fermentation and Bioindustrial Chemistry)  
 ST **chiroinosose** manuf Xanthomonas myoinositol oxidn; microbial  
 oxidn inositol **inosose** manuf  
 IT Oxidation  
 (biol.; microbial manuf. of chiro-**inosose** from myo-inositol)  
 IT Acetobacter  
 Acetobacteraceae  
 Agrobacterium  
 Enterobacter  
 Enterobacteriaceae  
 Erwinia  
 Fermentation  
 Gluconobacter  
 Haemophilus  
 Pasteurella  
 Pasteurellaceae  
 Pseudomonadaceae  
 Pseudomonas  
 Rhizobiaceae  
 Serratia  
 Sphingomonas  
 Xanthomonas  
 Yersinia  
 (microbial manuf. of chiro-**inosose** from myo-inositol)  
 IT **87-89-8**, myo-Inositol  
 RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study);  
 PROC (Process); RACT (Reactant or reagent)  
 (microbial manuf. of chiro-**inosose** from myo-inositol)  
 IT **56816-02-5P**, L-chiro-1-Inosose  
 RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL  
 (Biological study); PREP (Preparation)  
 (microbial manuf. of chiro-**inosose** from myo-inositol)

L12 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN  
 ACCESSION NUMBER: 2001:874389 CAPLUS  
 DOCUMENT NUMBER: 136:20217  
 TITLE: Preparation of L-**epi-inositol**  
 INVENTOR(S): Ogawa, Seiichiro; Takahashi, Atsushi  
 PATENT ASSIGNEE(S): Hokko Chemical Industry Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 22 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001335544	A2	20011204	JP 2000-158238	20000529
PRIORITY APPLN. INFO.:			JP 2000-158238	20000529
OTHER SOURCE(S):		CASREACT 136:20217; MARPAT 136:20217		

GI



AB Title compds. I (R1, R4-R7 = H, acyl, alkyl; if R2 = amino, acylamido, alkylamino, N-acyl-N-alkylamino, then R3 = H; if R2 = OH, acyloxy, then R3 = HOCH2, acyloxymethyl, azidomethyl, aminomethyl, acylamidomethyl; if R2 = O, then R3 = CH2 forming ring with R2) or their salts are prepd. L-Epi-2-inosose was reacted with PhNHNH2 in the presence of AcOH in H2O at 5.degree. for 2 h to give 79.5% L-epi-2-inosose phenylhydrazone, which was hydrogenated with H in the presence of platinum oxide in AcOH, treated with HCl at 100.degree. for 3.5 h, and treated with strongly acidic ion exchanger to give 2-amino-2-deoxy-L-**epi-inositol**.

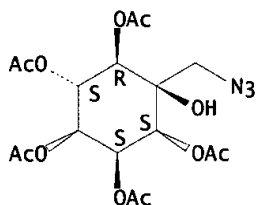
IT 377777-76-9P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of **epi-inositol**)

RN 377777-76-9 CAPLUS

CN D-epi-Inositol, 4-C-(azidomethyl)-, 1,2,3,5,6-pentaacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



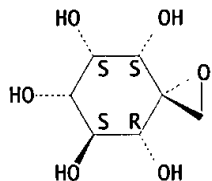
IT 22059-57-0P 38876-94-7P 377777-72-5P  
377777-74-7P 377777-77-0P 379224-06-3P  
379224-11-0P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of **epi-inositol**)

RN 22059-57-0 CAPLUS

CN D-epi-Inositol, 2,21-anhydro-2-C-(hydroxymethyl)- (9CI) (CA INDEX NAME)

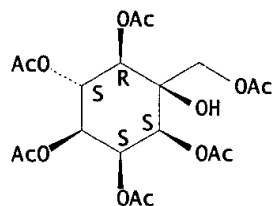
Absolute stereochemistry. Rotation (+).



RN 38876-94-7 CAPLUS

CN D-epi-Inositol, 4-C-[(acetyloxy)methyl]-, 1,2,3,5,6-pentaacetate (9CI)  
(CA INDEX NAME)

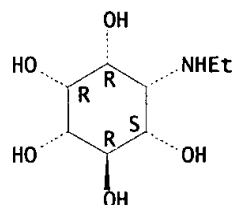
Absolute stereochemistry. Rotation (+).



RN 377777-72-5 CAPLUS

CN D-epi-Inositol, 4-deoxy-4-(ethylamino)- (9CI) (CA INDEX NAME)

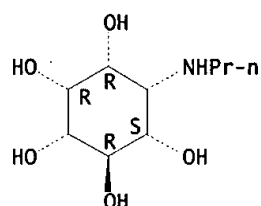
Absolute stereochemistry. Rotation (+).



RN 377777-74-7 CAPLUS

CN D-epi-Inositol, 4-deoxy-4-(propylamino)- (9CI) (CA INDEX NAME)

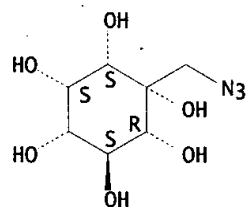
Absolute stereochemistry. Rotation (+).



RN 377777-77-0 CAPLUS

CN D-epi-Inositol, 4-C-(azidomethyl)- (9CI) (CA INDEX NAME)

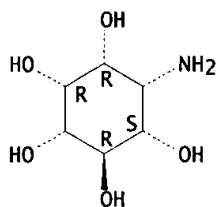
Absolute stereochemistry.



RN 379224-06-3 CAPLUS

CN D-epi-Inositol, 4-amino-4-deoxy- (9CI) (CA INDEX NAME)

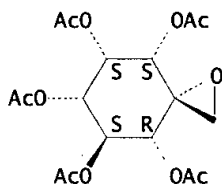
Absolute stereochemistry. Rotation (-).



RN 379224-11-0 CAPLUS

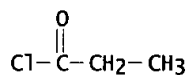
CN 1-Oxaspiro[2.5]octane-4,5,6,7,8-pentol, pentaacetate, (4R,5S,7S,8S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

IT 79-03-8, Propionyl chloride 100-63-0, Phenylhydrazine  
334-88-3, Diazomethane 33471-33-9, D-epi-4-  
InososeRL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of epi-inositol)

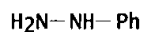
RN 79-03-8 CAPLUS

CN Propanoyl chloride (9CI) (CA INDEX NAME)



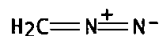
RN 100-63-0 CAPLUS

CN Hydrazine, phenyl- (8CI, 9CI) (CA INDEX NAME)



RN 334-88-3 CAPLUS

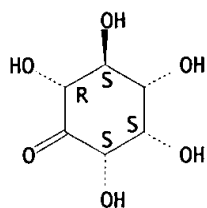
CN Methane, diazo- (8CI, 9CI) (CA INDEX NAME)



RN 33471-33-9 CAPLUS

CN D-epi-4-Inosose (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 7045-49-0P 377777-73-6P 377777-75-8P

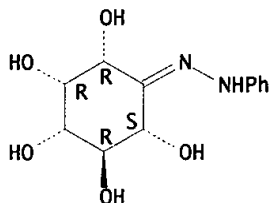
379224-07-4P 379224-09-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of epi-inositol)

RN 7045-49-0 CAPLUS

CN D-epi-4-Inosose, phenylhydrazone (9CI) (CA INDEX NAME)

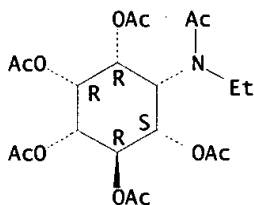
Absolute stereochemistry.



RN 377777-73-6 CAPLUS

CN D-epi-Inositol, 4-(acetyethylamino)-4-deoxy-, pentaacetate (ester) (9CI) (CA INDEX NAME)

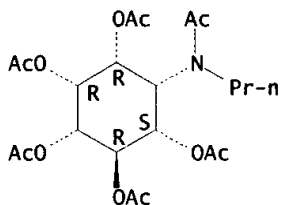
Absolute stereochemistry. Rotation (-).



RN 377777-75-8 CAPLUS

CN D-epi-Inositol, 4-(acetylpropylamino)-4-deoxy-, pentaacetate (ester) (9CI) (CA INDEX NAME)

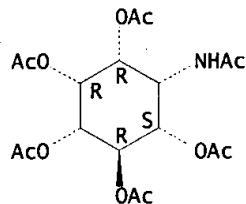
Absolute stereochemistry. Rotation (+).



RN 379224-07-4 CAPLUS

CN D-epi-Inositol, 4-(acetylaminopropyl)-4-deoxy-, 1,2,3,5,6-pentaacetate (9CI) (CA INDEX NAME)

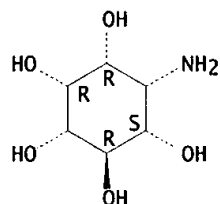
Absolute stereochemistry. Rotation (-).



RN 379224-09-6 CAPLUS

CN D-epi-Inositol, 4-amino-4-deoxy-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IC ICM C07C213-02

ICS C07C067-26; C07C069-21; C07C215-44; C07C233-23; C07C247-06;  
C07D301-02; C07D303-14; C07B061-00

CC 33-6 (Carbohydrates)

ST inositol prepn

IT 377777-76-9P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of epi-inositol)

IT 22059-57-0P 38876-94-7P 377777-72-5P

377777-74-7P 377777-77-0P 379224-06-3P  
379224-11-0P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of epi-inositol)

IT 79-03-8, Propionyl chloride 100-63-0, Phenylhydrazine

334-88-3, Diazomethane 33471-33-9, D-epi-4-Inosose

RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of epi-inositol)

IT 7045-49-0P 377777-73-6P 377777-75-8P

379224-07-4P 379224-09-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of epi-inositol)

L12 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:798044 CAPLUS

DOCUMENT NUMBER: 135:339209

TITLE: Compositions for inhibiting the proliferation of human immunodeficiency virus and method of inhibiting the proliferation of this virus

INVENTOR(S): Takeuchi, Tomio; Ohno, Tuneya; Nakamura, Mariko; Tamamura, Tsuyoshi; Takahashi, Atsushi

PATENT ASSIGNEE(S): Hokko Chemical Industry Co., Ltd., Japan; Zaidan Hojin



SOURCE: Biseibutsu Kagaku Kenkyu Kai  
PCT Int. Appl., 27 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001080848	A1	20011101	WO 2001-JP3587	20010425
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				

PRIORITY APPLN. INFO.: JP 2000-123407 A 20000425

AB (+)-Protoquercitol, (-)-protoquercitol, (.+-.)-protoquercitol, L-epi-2-  
**inosose**, D-epi-2-**inosose**, and DL-epi-2-**inosose**  
have an activity of inhibiting the proliferation of HIV infecting human T  
cells and/or human monocytes/macrophages and/or other human hemocytes and,  
therefore, are useful as HIV proliferation inhibitors. Also, a method of  
inhibiting the proliferation of HIV by treating HIV with the above compds.  
or enantiomers or racemates thereof, is provided.

IT 488-68-6, D-epi-2-**Inosose** 488-73-3,  
(+)-Proto-quercitol 6623-68-3, DL-epi-2-**Inosose**  
17278-12-5 33471-33-9, 2-**Inosose**, L-epi-  
90899-07-3

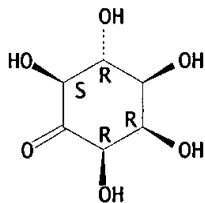
RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)

(quercitol and **inosose** analogs for inhibition of HIV  
proliferation)

RN 488-68-6 CAPLUS

CN D-epi-2-**Inosose** (7CI, 9CI) (CA INDEX NAME)

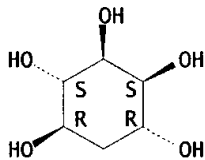
Absolute stereochemistry.



RN 488-73-3 CAPLUS

CN D-chiro-**Inositol**, 2-deoxy- (9CI) (CA INDEX NAME)

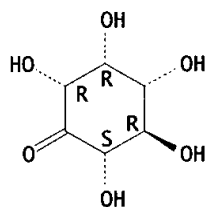
Absolute stereochemistry. Rotation (+).



RN 6623-68-3 CAPLUS

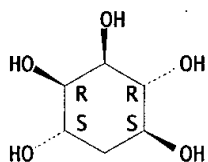
CN epi-2-**Inosose** (9CI) (CA INDEX NAME)

Relative stereochemistry.



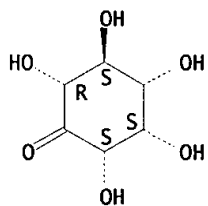
RN 17278-12-5 CAPLUS  
CN L-chiro-Inositol, 2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



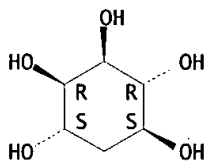
RN 33471-33-9 CAPLUS  
CN D-epi-4-Inosose (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 90899-07-3 CAPLUS  
CN chiro-Inositol, 2-deoxy- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IC ICM A61K031-047  
ICS A61K031-122; A61P031-18  
CC 1-5 (Pharmacology)  
Section cross-reference(s): 63  
ST quercitol inosose HIV proliferation inhibitor  
IT Hemocyte  
Macrophage  
Monocyte  
T cell (lymphocyte)  
(infection; quercitol and inosose analogs for inhibition of HIV proliferation)  
IT Drug delivery systems  
(injections; quercitol and inosose analogs for inhibition of HIV proliferation)  
IT Anti-AIDS agents

Human immunodeficiency virus 1  
(quercitol and inosose analogs for inhibition of HIV  
proliferation)

IT 488-68-6, D-epi-2-Inosose 488-73-3,  
(+)-Proto-quercitol 6623-68-3, DL-epi-2-Inosose  
17278-12-5 33471-33-9, 2-Inosose, L-epi-  
90899-07-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
(Uses)

(quercitol and inosose analogs for inhibition of HIV  
proliferation)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:24366 CAPLUS

DOCUMENT NUMBER: 134:171044

TITLE: (-)-epi-Inosose-2

AUTHOR(S): Hosomi, Hiroyuki; Ohba, Shigeru; Ogawa, Seiichiro;  
Takahashi, Atsushi

CORPORATE SOURCE: Faculty of Science and Technology, Department of  
Chemistry, Keio University, Kohoku-ku, Yokohama,  
223-8522, Japan

SOURCE: Acta Crystallographica, Section C: Crystal Structure  
Communications (2000), C56(12), e584-e585  
CODEN: ACSCEE; ISSN: 0108-2701

PUBLISHER: Munksgaard International Publishers Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The structure of the title compd., C<sub>6</sub>H<sub>10</sub>O<sub>6</sub>, was detd. to confirm the  
position of the keto group in the mol. prepd. enantioselectively by a  
bioconversion from myo-inositol. There are two independent mols. showing  
similar geometry. Crystallog. data are given.

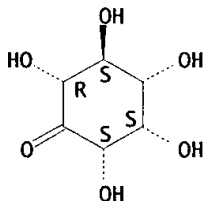
IT 33471-33-9, (-)-Epi-Inosose-2

RL: PRP (Properties)  
(crystal structure of)

RN 33471-33-9 CAPLUS

CN D-epi-4-Inosose (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 75-8 (Crystallography and Liquid Crystals)

Section cross-reference(s): 33

ST mol structure epi inosose

IT Crystal structure

Molecular structure  
(of epi-inosose-2)

IT 33471-33-9, (-)-Epi-Inosose-2

RL: PRP (Properties)  
(crystal structure of)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:881342 CAPLUS

DOCUMENT NUMBER: 134:42384

TITLE: Novel process for producing L-epi-2-inosose  
by microbial oxidation of myo-inositol and novel  
process for producing epi-inositol

INVENTOR(S): Takahashi, Atsushi; Kanbe, Kenji;  
Mori, Tetsuya; Kita, Yuichi;  
Tamamura, Tsuyoshi; Takeuchi, Tomio

PATENT ASSIGNEE(S): Hokko Chemical Industry Co., Ltd., Japan; Zaidan Hojin  
Biseibutsu Kagaku Kenkyu Kai

SOURCE: PCT Int. Appl., 65 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075355	A1	20001214	WO 2000-JP3687	20000607
W: CA, CN, IL, IN, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1197562	A1	20020417	EP 2000-937174	20000607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			JP 1999-159861	A 19990607
			JP 1999-340523	A 19991130
			JP 2000-151709	A 20000523
			WO 2000-JP3687	W 20000607

OTHER SOURCE(S): CASREACT 134:42384

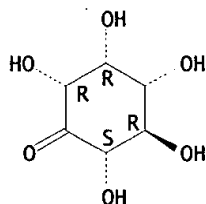
AB L-Epi-2-inosose and epi-inositol, which are useful as various drugs or synthesis intermediates, can be efficiently produced from less expensive myo-inositol. Myo-inositol is treated with a gram-neg. bacterium. e.g. Xanthomonas sp., capable of converting myo-inositol into L-epi-2-inosose to thereby convert the myo-inositol into L-epi-2-inosose. The L-epi-2-inosose thus obtained is further reacted in an aq. reaction medium with a reducing agent comprising an alkali metal boron hydride or another alkali metal hydride to form epi-inositol and myo-inositol. Next, the epi-inositol is sepd. and isolated from the redn. reaction mixt. comprising epi-inositol and myo-inositol to give epi-inositol.

IT 6623-68-3P, epi-2-Inosose  
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(novel process for producing L-epiinosose by microbial oxidn. of myo-inositol and boron hydride-redn. to epi-inositol)

RN 6623-68-3 CAPLUS

CN epi-2-Inosose (9CI) (CA INDEX NAME)

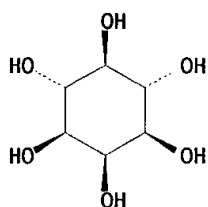
Relative stereochemistry.



IT 87-89-8, myo-Inositol  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(novel process for producing L-epiinosose by microbial oxidn. of myo-inositol and boron hydride-redn. to epi-inositol)

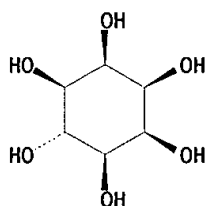
RN 87-89-8 CAPLUS  
 CN myo-Inositol (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 488-58-4P, epi-Inositol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (novel process for producing L-epiinosose by microbial oxidn.  
 of myo-inositol and boron hydride-redn. to epi-  
 inositol)  
 RN 488-58-4 CAPLUS  
 CN epi-Inositol (9CI) (CA INDEX NAME)

Relative stereochemistry.



IC C12P019-02; C12N001-20; C12P019-02; C12R001-64; C12P019-02; C12R001-38;  
 C12P019-02; C12R001-02; C12P019-02; C12R001-18; C12P019-02; C12R001-425;  
 C12P019-02; C12R001-21; C12P019-02; C12R001-01; C12N001-20; C12R001-64;  
 C12N001-20; C12R001-38  
 CC 33-6 (Carbohydrates)  
 Section cross-reference(s): 16  
 ST gram neg bacterium Xanthomonas microbial oxidn myoinositol;  
 epiinosose prepn redn; epiinositol prepn  
 IT Oxidation  
 (biol.; novel process for producing L-epiinosose by microbial  
 oxidn. of myo-inositol and boron hydride-redn. to epi-  
 inositol)  
 IT Acetobacter  
 Acetobacteraceae  
 Agrobacterium  
 Enterobacter  
 Enterobacteriaceae  
 Erwinia  
 Gluconobacter  
 Gram-negative bacteria  
 Haemophilus  
 Pasteurella  
 Pasteurellaceae  
 Pseudomonadaceae  
 Pseudomonas  
 Reduction  
 Rhizobiaceae  
 Serratia  
 Xanthomonas  
 Yersinia  
 (novel process for producing L-epiinosose by microbial oxidn.  
 of myo-inositol and boron hydride-redn. to epi-

- inositol)  
IT 6623-68-3P, epi-2-Inosose  
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(novel process for producing L-**epiinosose** by microbial oxidn. of myo-inositol and boron hydride-redn. to **epi-inositol**)
- IT 87-89-8, myo-Inositol  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(novel process for producing L-**epiinosose** by microbial oxidn. of myo-inositol and boron hydride-redn. to **epi-inositol**)
- IT 488-58-4P, epi-Inositol  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(novel process for producing L-**epiinosose** by microbial oxidn. of myo-inositol and boron hydride-redn. to **epi-inositol**)
- REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT